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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☒ Claim(s) *26-28 and 30* is/are allowed.

6)☒ Claim(s) *17-19,21,22,24 and 25* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed 04/28/08 has been entered.

Status of Claims

2) No claims have been amended via the papers filed 04/28/08.

Claims 17-22 and 24-30 are pending.

Claims 17-22, 24-28 and 30 are under examination.

Prior Citation of References

3) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) under 35 U.S.C § 103

4) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

5) The rejection of claims 17-19, 21, 22 and 25 made in paragraph 8 of the Office Action mailed 10/26/07 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al*. (*Vaccine* 10: 691-698, 1992, already of record) in view of Seid Jr. *et al*. (US 7,118,757, already of record) ('757) and O'Hagan (*J. Pharm. Pharmaco*. 50: 1-10, January 1998, already of record), is maintained for the reasons set forth therein and herein below.

Applicants allege that the Office: (i) has not established a *prima facie* case of obviousness as the Office has not shown that one of skill in the art would have had a reasonable expectation of success; (ii) has overstated the predictability of combining vaccine components with adjuvants; and (iii) has not cited to any portion of Seid ('757) that specifically teaches or suggests a combination of OMVs with capsular polysaccharide based composition. Applicants contend that at best the summary of the invention and column 4, lines 38-45 of Seid ('757) make sweeping statements regarding the OMVs, the purified OMP proteins and fragments thereof, as a broad group that may be able to be combined with other antigens such as capsular polysaccharides without clearly specifying if all such combinations are desirable or even possible. Applicants state that: (a) the first two full paragraphs of column 11 of Seid ('757) only refer to combination of the proteins or peptides with capsular components, OMVs being strikingly absent; (b) Example 1B is merely a protocol for preparing OMVs without any indication that they were to be combined with any other vaccine component; and (c) in Example 15, the inventors do actually combine capsular polysaccharides from serogroup C with an OMP derived peptide conjugate. This is allegedly very telling that 'the inventors did not think combining OMVs with capsular polysaccharides was desirable or even possible'. Applicants submit that Seid *et al*. ('757) had OMVs, had capsular polysaccharide conjugates, and had peptides, but only tried combining the capsular polysaccharide with the peptide even though they could have at the same time tested the capsular polysaccharide with the OMVs. Applicants further submit that combining vaccine components particularly from different classes, membrane vesicles versus capsular polysaccharides, can produce unpredictable results. Applicants point to Table 3 of the instant specification and state that the combination of the two antigens increases the immune response to OMV (NmB in the table) by more than 6-fold, but decreases the immune response to the capsular polysaccharide component by some

unknown amount (at least more than one third). Applicants further state that things become even more unpredictable with the addition of an adjuvant, and that O'Hagan is merely citing the best case results as MF59 does not always produce better results than alum. Applicants assert that despite the glowing praise for MF59 in O'Hagan, MF59 is not yet in any approved vaccine in the United States. Applicants state that the MF59 actually produces a lower immune response against the OMV components as shown in Table 3 of the specification. With this, Applicants opine that one cannot say that one of skill in the art would routinely select MF59 over alum especially given that it works less well with one of the two claimed components. Applicants cite case law and state that 'obvious to try' is not the standard under 35 U.S.C § 103. Applicants state that Costantino *et al*. used alum as an adjuvant so the Office must first posit some undisclosed flaw in Costantino *et al*. that would motive one of skill in the art to try a different adjuvant. Applicants argue that: (i) vaccines are not like a predictable mechanical art where there may be a general motivation to increase the immunogenicity to vaccines to ever increasing levels; and (ii) the immune system can be overstimulated which can cause averse reactions so a skilled practitioner will only seek to improve immunogenicity of a vaccine where there is demonstrated need. Applicants further submit that even if one of skill in the art were motivated to replace the alum in the oligosaccharide composition of Costantino *et al*., that is at best a suggestion that it would be obvious to try among all the available adjuvants to determine which if any would work better than aluminum hydroxide given that MF59 is not the only other adjuvant in existence. Applicants state that line 37 in column 12 through line 2 in column 13 of Seid ('513) identify at least six classes of adjuvants that include17 different adjuvants, and from this list alone, one of skill in the art would have seventeen adjuvants to test to see which if any may increase the antigenicity of the composition of Costantino *et al*. to better than that provided by the adjuvant already in the composition.

Applicants' arguments have been carefully considered, but are not persuasive. Contrary to Applicants' assertion, the Office did point to specific portions of Seid *et al*. ('757) disclosure that disclosed specific aspects of the instant invention. For instance, the Office identified various portions of Seid *et al.* ('757) in the rejection including 'Summary of the Invention' in column 2; paragraph bridging columns 3 and 4; Example 1B; first and

second full paragraphs in column 10; lines 38-45 in column 4; paragraph bridging columns 10 and 11; Examples 14 and 15; and Table 5B depicting MenC-CRM197 conjugate plus alum; Examples 10 and 14; the sentence bridging columns 9 and 10; and Table 5B depicting MenC-CRM197 conjugate plus alum; Examples 10 and 14; and first full paragraph in column 4. Particularly, the paragraph bridging columns 3 and 4 of Seid *et al.* ('757) taught that their invention pertains to vaccines comprising isolated OMVs of *Neisseria meningitidis*. The term 'comprising' is open claim language and includes therein other active elements and one or more adjuvants. Lines 28-30 of column 4 taught that at least one protein in Seid's ('757) vaccine is '**obtained in OMV formulation**' [Emphasis added]. Therefore, Seid's 'OMP' does not exclude, but expressly includes an OMP obtained in OMV formulation. See also line 1 of column 4. The isolated OMVs include those obtained from serogroup B *Neisseria meningitidis* strain H44/76 (B:15:P1,7.16). See Example 1B. The Office pointed to 'Summary of the Invention' in column 2 of Seid *et al*. ('757), the pertinent parts of which are reproduced herein below:

> The isolated OMV's … can be used in ….. multivalent subunit vaccines …. in mixtures …… In addition, isolated OMV's …. can be used in conjunction (as mixtures …. or conjugates) with other antigens of *N. meningitidis*. For example, ….. in conjunction with capsular polymers or oligomers (or fragments thereof) of *N. meningitidis* .....

The first full paragraph in column 4 taught that the polysaccharide vaccine can be 'enhanced' by a vaccine according to the invention as a vaccine with broad extensive action against most meningococcal serotypes. Seid's ('757) vaccine 'advantageously contains' meningococcal C polysaccharides 'covalently coupled to a protein or polypeptide carrier', such as, a non-toxin mutant or CRM, with or without aluminum hydroxide adjuvant. See lines 38-35 and 53-55 in column 4. Seid's ('757) proteins in the vaccine which include OMVs are used 'in connection with *other adjuvants* so that greater immunogencity is obtained' [Emphasis added]. See last sentence of the full paragraph in column 4. One specific example of a meningococcal C polysaccharide-CRM conjugate that is specifically disclosed by Seid *et al.* ('757) and encompassed in Seid's ('757) multivalent vaccine or mixture is MenC-CRM197 conjugate which further contains the adjuvant alum. See Table 5B for example. Thus, Seid's ('757) disclosure encompasses express suggestion of a vaccine comprising isolated meningococcal OMVs and advantageously containing therein a MenC-CRM197 conjugate in alum. Therefore,

Applicants' conclusions that OMVs are strikingly absent in the combination of Seid's ('757) proteins with capsular components and that Seid *et al*. did not think of combining OMVs with capsular polysaccharides, are inaccurate. Applicants appear to be arguing as though the reference of Seid *et al*. ('757) was applied as an anticipatory reference under 35 U.S.C § 102. However, Seid *et al*. ('757) was applied as a secondary reference under 35 U.S.C § 103(a). Applicants are further reminded that in order to qualify as art under 35 U.S.C § 103(a), Seid *et al*. ('757) do not have to exemplify under 'Examples' each and every embodiment taught therein. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations or references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc*., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Furthermore, with regard to Applicants' arguments on O'Hagan's express teaching that MF59-containing adjuvant is significantly more potent than alum inducing higher antibody titers in a number of animals compared to alum and that the use of the safe and more potent MF59 can be extended Group C meningococcal oligosaccharide-CRM197 conjugate vaccine, and Applicants' alleged unpredictable results depicted in Table 3 of the instant invention, the following should be noted. As presented currently, increases or decreases in immune response to the OMV or to the capsular polysaccharide conferred by MF59 are not a claim limitation in the instant claims. The claims as presented currently do not require that the MF59 adjuvant in the claimed immunogenic composition selectively increase or decrease immune response to one or both of the antigenic components present therein. O'Hagan specifically taught MF59-containing adjuvant to be significantly more potent than alum, inducing 5-50-fold higher antibody titers in a number of animals compared to alum. See abstract and paragraph bridging pages 5 and 6 of O'Hagan. From all clinical trials, O'Hagan concluded that M59 adjuvant is safe and effective in man in combination with a variety of antigens. Most importantly, O'Hagan taught that the range of antigens for which MF59 is effective was *extended to include* a polysaccharide-protein conjugate vaccine such as a Group C meningococcal oligosaccharide-CRM197 by Granoff *et al. Infect. Immun*. 65: 1710-1715, 1997. See left column on page 6 of O'Hagan and the reference of Granoff *et al*. cited at the end of left

column on page 9. It is particularly noted that consistent with the teachings of O'Hagan, Table 3 of the instant specification does show an increase in antibody titer to NmC when the MF59 adjuvant was added to NmC conjugate plus NmB OMV combination (a titer of >3375) compared to when alum was added to NmC conjugate plus NmB OMV combination (a titer of 2000). Furthermore, MF59 does not have to be approved in the United States in order for the reference of O'Hagan to qualify as a secondary reference under 35 U.S.C § 103. Instant claims do not require the recited MF59 to be a component of a vaccine that is approved in the United States. The instantly claimed immunogenic composition or vaccine is not limited to a vaccine that is approved in the United States. One of skill in that art would have readily recognized that O'Hagan's MF59 was not only known in the art to be a safe adjuvant, but significantly more potent than Costantino's alum. Applicants' argument that MF59 is not the only other adjuvant in existence, and that line 37 in column 12 through line 2 in column 13 of Seid ('513) identify at least six classes of adjuvants that include17 different adjuvants, and that from this list alone, one of skill in the art would have seventeen adjuvants to test to see which if any may increase the antigenicity of the composition of Costantino *et al*. to better than that provided by the adjuvant already in the composition, is irrelevant. The reference of Seid ('513) was not even applied as a part of this art rejection. With O'Hagan's specific comparison between MF59 and alum and with O'Hagan's express conclusion that M59-containing adjuvant is safe and significantly more potent than alum and that the range of antigens for which MF59 is effective was extended to include a polysaccharide-protein conjugate vaccine such as a Group C meningococcal oligosaccharide-CRM197, certainly one of ordinary skill in the art would NOT look into Seid's ('513) disclosure and test seventeen adjuvants to see which may increase the antigenicity of the composition of Costantino *et al*. Instead, as set forth previously, given the express teaching of Seid Jr. *et al*. ('757) that meningococcal OMV formulations can be used in conjunction with other antigens of *Neisseria meningitidis* including oligosaccharide or polysaccharide capsular components of serogroup C *Neisseria meningitidis* conjugated to a protein carrier such as non-toxic mutant CRM197, and the express teaching of O'Hagan that MF59-containing adjuvant is significantly more potent than alum, inducing higher antibody titers in a number of

animals compared to alum, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace alum in Costantino's group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate vaccine with O'Hagan's MF59 and then combine with Seid Jr.'s ('757) outer membrane vesicle vaccine formulation made from the group B meningococcal reference strain H44/76 to produce the instant invention. Given the express teaching of Seid Jr. *et al*. ('757) that the class 1 outer membrane proteins present in their group B meningococcal OMV formulations also occur in other groups including groups A, W-135 and Y meningococci and the express teaching by O'Hagan that the use of the safe and significantly more potent MF59 can be extended to Group C meningococcal oligosaccharide-CRM_{197} conjugate vaccine, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a mixed or multivalent vaccine that uses Seid Jr.'s ('757) H44/76 B *Neisseria meningitidis* outer membrane vesicles (OMVs) advantageously in conjunction with a group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate and provides broad, extensive action against most serotypes and is effective in preventing disease caused by group A, C, W-135 and Y as taught by Seid Jr. *et al*. ('757) and a vaccine that contains an adjuvant that is proved in the art to be safe and significantly more potent than alum as taught by O'Hagan. There is absolutely no teaching or indication in any of the applied references that replacing the less potent alum in Constantino's conjugate vaccine with the more potent MF59 adjuvant of O'Hagan would lead to overstimulation of one's immune system. Clearly, the Office has established a *prima facie* case of obviousness. The rejection stands.

6) The rejection of claim 24 made in paragraph 9 of the Office Action mailed 10/26/07 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al*. (*Vaccine* 10: 691-698, 1992, already of record) as modified by Seid Jr. *et al*. (US 7,118,757, already of record) ('757) and O'Hagan (*J. Pharm. Pharmaco*. 50: 1-10, January 1998, already of record) as applied to claim 17, and further in view of Seid (US 6,638,513, already of record) ('513), is maintained for the reasons set forth therein, herein below, and the paragraph immediately above.

Applicants contend that the addition of Seid ('513) fails to remedy the expectation of success as Seid ('513) fails to combine serogroup B OMVs with a capsular polysaccharide from serogroup C, and does not use MF59 in any form. Applicants state that Seid ('513) teaches polylactic acids as a possible alternative carrier, but states a preference for CRM_{197} and never actually uses polylactic acids. Applicants allege that the Office has provided no reason why one of skill in the art would want to use polylactic acids as the carrier *rather than* CRM_{197}. Applicants further opine that the proposed modification would render the composition of Costantino *et al*. unsuitable for the desired use. Costantino *et al*. allegedly states in the introduction on page 691 that the protein conjugate is specifically added to induce an immune response in very young children who do not produce a good antibody response to the capsular polysaccharide without the protein. Applicants point to MPEP 2143.01(V) which states that if proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the propose modification. Applicants argue that *replacing* the CRM_{197} carrier of Costantino *et al*. with a polylactic acid carrier would render the composition unsatisfactory to such young children as the toxoid protein is needed for the immune response in such children, so there can be no motivation to combine.

Applicants' arguments have been carefully considered, but are not persuasive. Applicants are reminded that the reference of Seid ('513) is not applied as an anticipatory art under 35 U.S.C § 102, but as a secondary reference under 35 U.S.C § 103. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations or references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc*., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. Contrary to Applicants' assertion, the Office provided the basis and sufficient technical reasoning for the rejection. No where does the Office's rejection state that one of skill in the art would want to use polylactic acids as the carrier *rather than* CRM_{197}. No where does the Office's rejection state that one of skill in the art would *replace* the CRM_{197} carrier of Costantino *et al*. with a polylactic acid carrier. Instead, the rejection of record stated that it would have been *prima facie* obvious to one of ordinary skill in the art

at the time the invention was made **to add** Seid's ('513) polylactic or polyglycolic acid to Costantino's immunogenic composition as modified by Seid Jr. *et al*. ('757) and O'Hagan to produce the instant invention, with a reasonable expectation of success. The rejection stated that one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Costantino's immunogenic composition as modified by Seid Jr. *et al*. ('757) and O'Hagan for primary vaccination without inducing the production of harmful antibodies as taught by Seid ('513). Therefore, the stated addition of Seid's ('513) polylactic or polyglycolic acid to Costantino's immunogenic composition as modified by Seid Jr. *et al*. ('757) and O'Hagan would not render the composition of Costantino *et al*. unsuitable for the desired use. Accordingly, MPEP 2143.01(V) has no relevance in the instant rejection. The rejection stands.

Relevant Prior Art

7) The art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- At the time of the instant invention, Granoff *et al*. (*Infect. Immun*. 65: 1710-1715, May 1997) taught the following with regard to the immunity-augmenting or immunity-accelerating properties of the MF59 adjuvant compared with alum (see page 1714) [Emphasis added]:

> The most important finding of this study is that MF59, an adjuvant that has been **widely evaluated in humans** with a variety of glycoprotein subunit vaccines and inactivated influenza vaccines, both *accelerates and augments* serum anti-PS antibody responses of infant baboons immunized with Hib and ***N. meningitidis* group C PS-protein conjugate vaccines**. In addition, the animals vaccinated with the MF59-adjuvanted vaccines showed higher titers during the extended follow-up period. These animals also were capable of mounting memory serum antibody responses to unconjugated *N. meningitidis* group C and Hib PS booster immunizations. The immunologic priming appeared to be similar in the animals primed with the conjugate vaccine administered either with alum or MF59 (Fig. 2C).
>
> In summary, the excellent immunogenicity of *N. meningitidis* group C and Hib conjugate vaccines when administered with MF59 to infant baboons and the lack of apparent toxicity are **consistent with the excellent immunogenicity and safety record of MF59 used with other vaccines in clinical trials in humans** (summarized in the introduction). These data, together with the potential of an adjuvant either to permit the use of lower conjugate vaccine dosages and/or fewer injections or **to enhance the immunogenicity of multicomponent PS-protein conjugate vaccines given** alone or **in combination with other vaccines**, support the initiation of phase I safety and immunogenicity trials of MF59 and glycoconjugate vaccines in humans.

Granoff's teachings do not represent or suggest unpredictability in combining MF59 adjuvant with a multicomponent PS-protein conjugate vaccine given in combination with other vaccines.

Remarks

8) Claims 17-19, 21, 22, 24 and 25 stand rejected. Claims 20 stands objected to as being dependent from a rejected claim. Claims 26-28 and 30 are allowable.

9) This is a continuation (RCE) of Applicant's earlier Application No. 09701453. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

11) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-

217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

12) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Acting supervisor, Shanon Foley, can be reached on (571) 272-0898.

/S. Devi/
S. Devi, Ph.D.
Primary Examiner
AU 1645

July, 2008